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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,201	07/21/2003	David J. Hannapel	82162/171 (ISURF #02885)	1454

7590 09/23/2005

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 09/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/624,201	HANNAPEL ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *26-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7-12,14,15,17-19,21,22,24,25,43,45,46,48-50,52,53,55 and 56* is/are rejected.

7)☒ Claim(s) *2,5,6,13,16,20,23,44,47,51 and 54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/8/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-56 are pending.

2. Applicant's election with traverse of Group I, claims 1-25 and 43-56, to the extent they are drawn to SEQ ID NO:1 encoding SEQ ID NO:2 in the reply filed on 7/11/2005 is acknowledged. The traversal is on the ground(s) that the claims of the present application are closely related and, therefore, would require common areas of search and consideration.

This is not found persuasive because while the search of the prior art for one group may overlap with that of another, they are not co-extensive of each other and thus would be a burden on the Office.

The requirement is still deemed proper and is therefore made FINAL.

Claims 26-42 are withdrawn from consideration for being drawn to non-elected inventions.

3. Claims 1-25 and 43-56 to the extent they are drawn to SEQ ID NO:1 encoding SEQ ID NO:2 are examined in the present office action.

Claim Objection

4. Claims 2-6, 13-16, 20-23, 44-47, and 51-54 are objected to for being drawn to non-elected inventions. The objection includes dependent claims. Correction is requested.

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See for example page 16, line 24. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 48 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 48 and 55 recite the limitation "wherein the first nucleic acid molecule" in claims 43 and 50, respectively. There is insufficient antecedent basis for this limitation in the claim.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 3-4, 7-12, 14-15, 17-19, 21-22, 24-25, 43, 45-46, 48-50, 52-53, and 55-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid molecule encoding a BEL transcription factor from *Solanum tuberosum*, or wherein said nucleic acid molecule encodes a protein that is at least 85% similar to a homeodomain region, a SKY box, a BELL domain, and a VSLTLGL-box in SEQ ID NO:2, or wherein the nucleic acid molecule hybridizes to the nucleic acid sequence of SEQ ID NO:1 under stringent conditions comprising 5X SSC at 55^0C; a DNA construct, expression vector, host cell, transgenic plant, transgenic plant seed, a method for enhancing growth in a plant, and method for regulating flowering in a plant, comprising said nucleic acid molecule.

Applicants disclose the isolation of StBEL-05 from *Solanum tuberosum* using a two-hybrid selection system in yeast using the POTH1 (potato homeobox cDNA) in the GAL4-binding domain vector (page 89, lines 20-31). Applicants disclose the cDNA sequence of StBEL-05 is set forth in SEQ ID NO:1 encoding the deduced amino acid sequence of SEQ ID NO:2 (page 22, paragraphs 55-56). Applicants disclose that StBEL-05 is a novel BEL type of transcription factor in the TALE superclass. StBEL-05 comprises a homeodomain region encompassing helices I, II, and III, the amino-terminal SKY box consisting of 20 amino acids (from ser 207 to lys-226 in StBEL-05), the 120 amino acid domain starting at leu-272 of the StBEL-05 sequence, and the carboxy-terminal VSLTLGL-box (SEQ ID NO:15) beginning at val-620 (paragraph 164, bridging pages 90-91). The deduced lengths of the seven original cDNAs isolated in the yeast two-hybrid screen are 688 aa for StBEL-05, 535 aa for StBEL-11,

586 aa for StBEL-13, 589 aa for StBEL-14, 620 aa for StBEL-22, 567 aa for StBEL-29, and 645 aa for StBEL-30. Five'-RACE was used to verify the full-length of StBEL-05, -13, -14 and -30. Southern blot analysis revealed that these genes are unique and belong to small gene subfamilies, based on the complexity of bands detected by gene-specific probes from each of the cDNAs (Figure 13C) (page 91, paragraph 165).

The Applicants do not identify essential regions that are unique to StBEL-05 proteins encoded by SEQ ID NO:1, nor do Applicants describe any polynucleotide sequences that encode any BEL transcription factor, or encodes any BEL transcription factor that hybridizes to SEQ ID NO:1 under stringent conditions and encodes a protein with the same activity and function as the StBEL-05 protein encoded by SEQ ID NO:1.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences encoding a StBEL-05 protein falling within the scope of the claimed genus of polynucleotides which encode any BEL transcription factor, or encode a BEL transcription factor wherein the protein is at least 85% similar to any homeodomain region, a SKY box, a BELL domain and a VSLTLGL-box in SEQ ID NO:2, or wherein the nucleic acid hybridizes under stringent conditions to SEQ ID NO:1. Applicants only describe a single cDNA sequence of SEQ ID NO:1. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the StBEL-05 protein, it remains unclear what features identify a StBEL-05 protein. Since the genus of StBEL-05 proteins has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Scope of Enablement

8. Claims 1, 3-4, 7-12, 14-15, 17-19, 21-22, 24-25, 43, 45-46, 48-50, 52-53, and 55-56 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule of SEQ ID NO:1 encoding the polypeptide of SEQ ID NO:2, a DNA construct and expression vector comprising said isolated nucleic acid molecule; and host cell, transgenic plant, and transgenic plant seed transformed with the isolated nucleic acid molecule, does not reasonably provide enablement for an isolated nucleic acid molecule encoding a BEL transcription factor from *Solanum tuberosum*, or wherein said isolated nucleic acid molecule encodes a protein that is at least 85% similar to any homeodomain region, a SKY

box, a BELL domain and a BSLTLGL-box in SEQ ID NO:2, or wherein said isolated nucleic acid molecule hybridizes to SEQ ID NO:1 under stringent hybridization conditions and host cells and plants transformed therewith or methods comprising said nucleic acid molecule; or Applicants are not enabled for a method of enhancing growth in a plant or method for regulating flowering in a plant comprising transforming a plant with SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to an isolated nucleic acid molecule encoding a BEL transcription factor from *Solanum tuberosum*, or wherein said nucleic acid molecule encodes a protein that is at least 85% similar to a homeodomain region, a SKY box, a BELL domain, and a VSLTLGL-box in SEQ ID NO:2, or wherein the nucleic acid molecule hybridizes to the nucleic acid sequence of SEQ ID NO:1 under stringent conditions comprising 5X SSC at 55^0C, or wherein the nucleic acid molecule is SEQ ID NO:1 or the nucleic acid molecule encodes SEQ ID NO:2; a DNA construct, expression vector, host cell, transgenic plant, transgenic plant seed, a method for

enhancing growth in a plant, and method for regulating flowering in a plant, comprising said nucleic acid molecule.

Applicants disclose the isolation of StBEL-05 from *Solanum tuberosum* using a two-hybrid selection system in yeast using the POTH1 (potato homeobox cDNA) in the GAL4-binding domain vector (page 89, lines 20-31). Applicants disclose the cDNA sequence of StBEL-05 is set forth in SEQ ID NO:1 encoding the deduced amino acid sequence of SEQ ID NO:2 (page 22, paragraphs 55-56). Applicants disclose that StBEL-05 is a novel BEL type of transcription factor in the TALE superclass. StBEL-05 comprises a homeodomain region encompassing helices I, II, and III, the amino-terminal SKY box consisting of 20 amino acids (from ser 207 to lys-226 in StBEL-05), the 120 amino acid domain starting at leu-272 of the StBEL-05 sequence, and the carboxy-terminal VSLTLGL-box (SEQ ID NO:15) beginning at val-620 (paragraph 164, bridging pages 90-91). The deduced lengths of the seven original cDNAs isolated in the yeast two-hybrid screen are 688 aa for StBEL-05, 535 aa for StBEL-11, 586 aa for StBEL-13, 589 aa for StBEL-14, 620 aa for StBEL-22, 567 aa for StBEL-29, and 645 aa for StBEL-30. Five'-RACE was used to verify the full-length of StBEL-05, -13, -14 and -30. Southern blot analysis revealed that these genes are unique and belong to small gene subfamilies, based on the complexity of bands detected by gene-specific probes from each of the cDNAs (Figure 13C) (page 91, paragraph 165). Applicants disclose that a 2000-bp fragment of the coding sequence of StBEL-05 in a sense orientation driven by the CaMV-35S promoter was transformed into potato (page 94, paragraph 169). The highest expressers of StBEL-05 sense transcripts exhibited tuber formation under LD conditions whereas control plants produced tubers only under SD conditions. The highest overexpressers of StBEL-05 also produced more

tubers than control plants and were more responsive to inductive conditions. Tubers from overexpressers grew larger than controls. Applicants disclose that plants overexpressing StBEL-05 were taller and had a greater weight compared to control plants (page 97, Table 4).

Re: claim 43 is drawn to a method for enhancing growth, but Applicants have not defined this term. Therefore, the Office interprets this term to encompass disease resistance and photosynthesis capacity for example. Applicants are not enabled for the full breadth of "enhanced growth". Applicants are enabled for a method of increasing the growth rate of a plant, or increasing the number and size of potato tubers comprising transforming a plant with SEQ ID NO:1.

Re: claim 50 is drawn to a method for regulating flowering in a plant. Applicants have not disclosed by way of example or disclosure, that their invention has any effect or influence on flowering.

Applicants claims are drawn to nucleic acid sequences that hybridize to SEQ ID NO:1, but the state-of-the-art teaches isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2^{nd} paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking

into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2).

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids that hybridize under stringent conditions to SEQ ID NO:1 will encode a protein with the same activity as a protein encoded by SEQ ID NO:1. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (McConnell et al, Nature 411 (6838):709-713, 2001, see especially page 710, left column, 2nd paragraph).

The state-of-the-art teaches that transforming plants with homeobox transcription factors produces unexpected results. Chuck et al (1996, The Plant Cell 8:1277-1289) teach transforming Arabidopsis plants with the Arabidopsis knotted1-like gene, KNAT1, produced plants with abnormal phenotypes. The transformed plants exhibited large, severely lobed leaves, some of which comprised ectopic shoot meristems in the sinus region, small flowers with thin, elongated, greenish petals that abscised early and anthers that dehisced later than normal, and vascular tissue that developed aberrantly (page 1278, left column, 1st paragraph of results; page 1279, Figure 1C and right column; page 1280, left column, 1st paragraph).

Applicants have not disclosed how one makes or isolates any of the sequences that are encompassed by Applicants' broad claims. Applicants have not taught which regions of the respective polynucleotides can be used to amplify any of said polynucleotides or which regions can be used as a probe to isolate any of said polynucleotide sequences.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:1 as probes or by designing primers to undisclosed regions of SEQ ID NO:2 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed produce a potato plant with increased number and weight of tubers.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claim 11 is directed to non-statutory subject matter. This rejection is made because the claims are drawn to "a mammalian cell" which reads on a human being. Amending the claim to recite "isolated mammalian cell" will obviate the rejection.

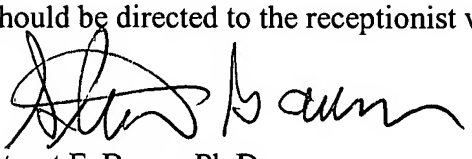
10. Claims 2, 5-6, 13, 16, 20, 23, 44, 47, 51, 54 are objected to.

11. Claims 1, 3-4, 7-12, 14-15, 17-19, 21-22, 24-25, 43, 45-46, 48-50, 52-53, 55-56 are rejected.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on 571-272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
September 12, 2005